CLAIMS

We claim:

1. An amino acid composition with improved blood brain barrier permeability comprising a chemically synthesized amino acid polymer, wherein the amino acid polymer comprises at least one asparagyl-4-aminobutane or glutamyl-4-aminobutane residue.

2. The composition of claim 1, additionally comprising an imaging agent, wherein the imaging agent is sufficient for imaging of the composition in a medical imaging diagnostic procedure.

3. The composition of claim 1 wherein the amino acid polymer is a protein or peptide comprising between 10 and 40 amino acid residues.

4. The composition of claim 1 wherein the amino acid polymer is a protein and peptide of between 40 and 80 residues.

5. The composition of claim 1 wherein the amino acid polymer is a protein or peptide of between 3-10 residues.

6. The composition of claim 1, wherein the amino acid polymer is part of a multi-subunit protein.

7. The composition of claim 1, wherein the amino acid polymer is an immunoglobulin or fragment of an immunoglobulin.

8. The composition of claim 2 wherein the medical imaging diagnostic procedure is magnetic resonance imaging.

9. The composition of claim 8 wherein the imaging agent comprises a molecule selected from the group consisting of Gd, Fe and Dy.

10. The composition of claim 9 wherein the imaging agent comprises Gd-DTPA aminohexanoic acid.

11. The composition of claim 2 wherein the imaging agent is selected from paramagnetic CEST agents.

12. The method of claim 11 wherein the agent is selected from the group consisting of Eu^{+3}, Tb^{+3}, Dy^{+3}, Er^{+3}, Tm^{+3}, and Yb^{+3}.

13. The composition of claim 2 wherein the imaging agent is selected from the group consisting of ^{123}I, ^{18}F, ^{111}In, ^{67}Ga, ^{99m}Tc, ^{11}C, ^{89}Zr, ^{90}Y, and ^{177}Lu.

14. The composition of claim 1 wherein the amino acid polymer comprises a sequence identical to at least the first 25 amino acid residues of the human

amyloid-β peptide with the substitution of asparagyl-4-aminobutane and glutamyl-4-aminobutane in at least one Asp or Glu position.

15. The method of claim 1 wherein the polymer is identical to at least the first 30 residues.

16. The method of claim 1 wherein the polymer is identical to at least the first 35 residues.

17. The method of claim 1 wherein the polymer is identical to at least the first 40 residues.

18. The composition of claim 14 wherein the amino acid polymer comprises at least 5 asparagyl-4-aminobutane or glytamyl-4-aminobutane residues.

19. A method of creating an amino acid polymer with improved blood brain barrier permeability comprising the steps of chemically synthesizing an amino acid polymer, wherein at least one asparagyl-4-aminobutane or glutamyl-4-aminobutane residue is incorporated within the amino acid polymer.

20. The product of the method of claim 13.

21. The product of claim 20, additionally comprising an imaging agent, wherein the imaging agent is sufficient for imaging of the composition in a medical imaging diagnostic procedure.

22. The product of claim 20 wherein the amino acid polymer is a protein or peptide comprising between 10 and 40 amino acid residues.

23. The product of claim 20 wherein the amino acid polymer is a protein and peptide of between 40 and 80 residues.

24. The product of claim 20 wherein the amino acid polymer is a protein or peptide of between 3-10 residues.

25. The product of claim 20, wherein the amino acid polymer is part of a multi-subunit protein.

26. The product of claim 20, wherein the amino acid polymer is an immunoglobulin or fragment of an immunoglobulin.

27. The product of claim 21 wherein the medical imaging diagnostic procedure is magnetic resonance imaging.

28. The product of claim 27 wherein the imaging agent comprises a molecule selected from the group consisting of Gd, Fe and Dy.

29. The product of claim 21 wherein the imaging agent comprises Gd-DTPA aminohexanoic acid.

30. The product of claim 21 wherein the imaging agent is selected from paramagnetic CEST agents.

31. The method of claim 30 wherein the agent is selected from the group consisting of Eu^{+3}, Tb^{+3}, Dy^{+3}, Er^{+3}, Tm^{+3}, and Yb^{+3}.

32. The composition of claim 21 wherein the imaging agent is selected from the group consisting of ^{123}I, ^{18}F, ^{111}In, ^{67}Ga, ^{99m}Tc, ^{11}C, ^{89}Zr, ^{90}Y, and ^{177}Lu.

33. The product of claim 20 wherein the amino acid comprises a sequence identical to at least the first 25 amino acid residues of the human amyloid-β peptide with the substitution of asparagyl-4-aminobutane and glutamyl-4-aminobutane in at least one Asp or Glu position.

34. The product of claim 33, wherein the polymer is identical to at least the first 30 residues.

35. The product of claim 33, wherein the polymer is identical to at least the first 35 residues.

36. The product of claim 33, wherein the polymer is identical to at least the first 40 residues.

37. The product of claim 33 wherein the amino acid chain comprises at least 5 asparagyl-4-aminobutane or glytamyl-4-aminobutane residues.

38. A method of synthesizing N-α-Fmoc-L-aspartyl-γ-(4-aminobutyl)-carbamic acid tert-butylester or N-α-Fmoc-L-glutamyl-δ-(4-aminobutyl) carbamic acid tert butyl ester comprising the steps of:

(a) dissolving N-α-Fmoc-L-aspargyl α-allyl ester or N-α-Fmoc-L-glutamyl α-allyl ester in a solvent,

(b) adding sequentially an activating agent and a weak base, stirring and cooling,

(c) while stirring, adding (4-aminobutyl) carbamic acid ter-butyl ester,

(d) removing the solvent,

(e) dissolving the residue in water and acidifying with acid,

(f) extracting the aqueous phase,

(g) washing with aqueous inorganic weak base and brine and drying,

(h) adding a nonpolar solvent and cooling, which results in the formation of a precipitate,

wherein the precipitate comprises N-α-Fmoc-aspartyl-γ-(4-aminobutyl) carbamic acid tert-butyl ester α-allyl ester or N-α-Fmoc-L-glutamyl acid δ-(4-aminobutyl) carbamic acid tert-butyl ester α-allyl ester,

(i) suspending the precipitate in a solvent and stirring,

(j) adding a transition metal catalyst and stirring,

(k) removing the solvent and washing the aqueous layer with an organic solvent and acidifying the aqueous phase with an acid, and

(l) isolating the precipitate.